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RADIUM

EDITED BY
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VOL. XV MAY, 1920 No. 2

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

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RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D. with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. XV MAY, 1920 No. 2

REVIEWS AND ABSTRACTS

John G. Clark, M.D. and Floyd E. Keene, M.D., (Philadelphia). Radiation in Inoperable Cases of Carcinoma in the Female Genito-Urinary Organs. The American Journal of Roentgenology, vii, 36-41, January, 1920. Read at the Third Annual Meeting of the American Radium Society, Atlantic City, N. J., June 5, 1919.

"One year ago we presented a summary of results in 100 cases of inoperable cancer of the cervix and female genital organs treated in the Gynecological Department of the University Hospital, and arrived at the following conclusions:"

"'1. As a palliative remedy, radium is the treatment par excellence in inoperable cases of cancer of the cervix."

"'2. In border-line cases, in which formerly we accepted the grave risks of an operation in the hope of eradicating the disease, we now employ radium; but in the certainly operable class we will advocate a radical operation followed by post-operative radiation."

"'3. In cancer of the fundus, even when far advanced, we perform a hysterectomy, resorting to radiotherapy only in the face of grave operative contra-indications.'"

"Our fourth conclusion, which in view of our further experience, we now feel may be modified by a limited claim for actual curability, was as follows:"

"'4. As yet we claim no cures, but, based upon the observation of a considerable number of inoperable cases which have remained locally healed from one to three years, we venture the hope that the quinquennial test will find several survivors.'"

"Our list now comprises 209 cases since 1913 with the following results:"

	Dead	*Not Traced*	*Living*
1914	8	0	1
1915	19	1	4
1916	46	8	11
1917	33	3	23
1918	5	13	34
Total	111	25	73

"We regret that we are unable at this stage of our report to give a more complete summary owing to the fact that the number of patients not traced is accounted for by two conditions incident to war; first, the decreased number of our hospital staff, rendering it impossible to keep our follow-up system up to date,—and second, the nomadic tendency of an urban population, due to the recent fluctation of our industrial system and the disturbance incident to the housing situation. In endeavoring to trace our patients we have not infrequently found a change of three or more addresses within a few months after their discharge from the hospital. Notwithstanding such omissions in our reports, the showing in this series is rather remarkable, and we have been greatly encouraged to find so large a number of patients, all of whom fell within the inoperable class, still living and apparently well many months subsequent to their last treatment. A number of these cures have been startling; we believe we are justified in our hopes for some permanent cures, and we know beyond cavil that the palliative results have been far and away better than those following any therapeutic measures hitherto employed. In reviewing our results from radium therapy, we find that same bizarre tendency as noted in our previous surgical experience with cancer. From the appearance or even the extent of the disease no one can forecast with assurance the probable outcome of treatment."

"When surgical measures are invoked, one frequently ends an operation with a great degree of optimism as to a cure, because the disease has apparently been well circumscribed and has shown no demonstrable metastasis, and yet within a few months it has again appeared with renewed violence at the local site of operation, while in another case, when the frontier zone of the growth has not been satisfactorily encompassed and the prognosis is bad, the patient may remain free a long time from recurrence or may even be cured. This same peculiarity has been noted in our radium experience. Thus in our 9 cases treated in 1914, the one living patient discredited every forecast and survives today, and is to all appearances cured despite a very extensive and a very vicious type of cancer."

"A young woman under thirty years of age was taken into one of our hospitals in an almost moribund state from a massive intraperitoneal hemorrhage, incident to a large perforation of the fundus of the uterus from a decidnoma malignum. The surgeon was compelled because of the critical state of the patient to perform a rapid supravaginal hysterectomy. Her convalescence was slow; she left the hospital in a very precarious condition and was readmitted six weeks later almost ensanguinated from a massive vaginal hemorrhage. On examination, a large fixed mass was found in the left side of the pelvis, and a deep irregular crater occupied the site of the cervix. A hasty cauterization was done to save her life. Notwithstanding the hopeless outlook, two applications of 100 milligrams of radium were made at a six weeks' interval. After the first radiation the bleeding ceased and her recovery was nothing less than

astounding. This patient's five-year period has been reached, and she is now well and actively engaged in her household duties and has adopted a child. Were we to let this case occupy the center of the limelight and ignore the cases within the shadow a very brilliant argument could be constructed in favor of radium; but surgery has just as remarkable instances of unexpected cures, and we must, therefore, turn to a summary of all cases in order to find a judicial equilibrium. In these startling cases, however, we feel that there may be further guides towards still better results. Possibly through the use of radium or its emanation carried into the depth of a growth a further advance may be made. At least these remarkable cases furnish a further sustaining argument in favor of the cure of cancer so long as the process is still localized and without metastasis when it is attacked either by surgical means or radium."

"Other cases in our series are equally noteworthy. It is not our purpose, however, to lay great stress upon these highly gratifying isolated instances, but to base our discussion upon the influence of radium in those patients who are not healed. Time will soon establish the question of final cures. In the meantime we feel that a very important advance has been made in the palliative treatment of even the hopeless cases. Thus, in our cases hemorrhage has almost invariably been stopped for a considerable period, in some never returning, in others recurring at variable periods before the death of the patient. In still others it has been notably lessened, and but seldom has it not been influenced. No argument is required to confirm this beneficent palliation in the case of fear-stricken women, for to those who witness it the results are self-evident. The malodorous discharges are likewise eliminated in a considerable proportion of cases. As to its alleviatory influence on pain we cannot claim so much, and yet it frequently acts most happily in this direction. In radium cases, as in surgery, however, we must meet lay criticism as well as professional pessimism where pain is not relieved after radiation, or comes on later in the course of the inoperable case. Frequently this acute terminal agony is charged up to the account of radiation by relatives or friends of the patient, and occasionally the objection to the use of this novel remedy is sustained by the family physician. Every surgeon knows that surgery is likewise condemned under the same conditions. In all propaganda work, therefore, among laymen as well as within our professional circle, the fact should be emphasized that while cancer in its earlier stages is always painless, in its terminal stages it is nearly always agonizing. In this way only may false assumptions concerning any remedy which fails be overcome. In the occasional case in our series in which the pain has been especially severe, we have felt that possibly there might be a shadow of suspicion in support of this hypothesis; and yet within a few days another case may be seen with identical symptoms in which no treatment whatever has been applied. Even admitting such possibility in the occasional case, the many others which have found relief from pain easily overbalance these objections."

"Finally, are there any untoward sequellae chargeable to the radium account? Two are possible. First, does radiation produce pain shortly after the first or second sitting? Occasionally it does. In anticipation of this possibility, we warn the patient not to be alarmed should it occur, for in a small percentage of cases, notwithstanding every care exercised in the protection of the rectum, a very acute proctitis may follow. In such cases, a decided stranguary may be noted at variable intervals, from

a few days to three or more weeks, after radiation. Mucous and even blood may be discharged and the pain may be so severe as even to require hypnotics. In some cases opium suppositories may be necessary to quiet the patient. In others, a mucilagenous suspension of bismuth subnitrate by rectal injection may be quite sufficient to soothe the pain. In general, however, this symptom is the exception rather than the rule and will be noted less and less frequently as precaution is observed in the protection of the rectum and bladder. Still less frequently is vesical tenesmus noted, and as a rule it is of a more evanescent type."

"As to fistula, we have noted seventeen, nine recto-vaginal and eight vesical. By no means should all of these fistulae be charged to radium, for in over 200 cases of inoperable cancer which are not treated, this terminal event will certainly occur in a larger number of patients. We are convinced, therefore, that such distressing phases of cancer of the cervix are actually prevented, for in the large number of cases of deep ulcerating cervical craters, which were locally healed, there has been no further trouble in this locality, the patient ultimately dying of metastasis or deep pelvic extension."

"Briefly stated, therefore, we see in the use of radium in inoperable cases of cancer a greater tendency to relieve pain than to produce it, and also a smaller percentage of fistulae after its use than in the patients going to their death untreated, or after various palliative operations have been performed or the actual cautery has been applied. Through the results achieved by radiation in this group of inoperable cases the question is forced into the foreground: Shall we abandon the radical operation in all cases in favor of radiation? As yet, we cannot wisely answer it. Certainly the questionable operative case must be transferred to radium therapy. In the definitely operable case with a well-circumscribed area and no broad ligament extension, we still advise hysterectomy and follow this procedure in about fourteen days later with a 100 milligram application of radium for twelve hours. We base this adherence upon the certainty of a definite percentage of cures obtained through surgical intervention. On the other hand, the transfer of the questionable case to the less drastic procedure is based upon the certainty of a large surgical mortality, the frequency of disabling sequellae and the distressingly high percentage of recurrence after even the most radical operation."

"Thus far we know that radium effectively supplements surgery, and within the next five years it may possibly supplant the radical operation in even the early case."

"Finally, as to the question of operation after radium has reduced the inoperable to apparently an operable stage: Upon this issue we find no reason to change our position as formerly expressed, for there is no convincing argument in favor of this plan. We feel convinced that surgery can accomplish nothing further: on the contrary, we believe that surgical intervention is most hazardous. The connective tissue contractures in the vaginal vault and parametrium incident to radiation must render the dangers of injury to the bladder, ureters, and rectum greater, and the disruption of connective tissue which may actually have encapsulated the carcinoma may lead to a reimplantation of malignant cells, which may have been held in leash or have actually been rendered inocuous. On the other hand, in the positively operable cases we commend the plan advocated by Howard Taylor. He radiates all operable cases a few days before hysterectomy is performed. This appears most logical, for he intervenes before the actual destructive changes have taken place

and in his experience finds no increase in the difficulty of a panhysterectomy. This, however, is a very different proposition from that offered after a deep crater has been apparently healed and upon its site dense hyalinized tissue has formed which drags the base of the bladder, ureters and rectum into close juxtaposition."

TECHNIQUE

"As to technique, we have not varied from that described in preceding articles. One hundred milligrams are applied at one sitting and repeated at a second interval six or eight weeks later. If no improvement is noted after the second sitting, we make no further application, as we have seen no benefit accrue from a third treatment when the two preceding have failed."

"Our technique is a simple one. The silver or platinum radium containers, as they come from the radium laboratories, are encased in black rubber drainage tubing, carefully tied at both ends. The site of the cancer must be exposed with one or two Syms' specula, as necessity demands. Usually a gauze tampon which forms a buffer between the rectum and the cancerous area is carefully applied and upon this the radium tubes rest transversely to the axis of the vagina. Above, the radium gauze is further packed to protect the bladder, followed by a liberal but not uncomfortable gauze tampon within the vagina. Frequently the vaginal vault may be much more expeditiously exposed by placing the patient in the Syms' or knee-breast posture. Indeed, in some instances, the latter posture greatly facilitates the more accurate placing of the radium tubes. The patient usually remains in the hospital one or two days."

"In only one case has anything untoward occurred immediately after the application. This patient was greatly depleted by hemorrhage, and a deep crater under the bladder was present. Soon after radiation she developed all of the active symptoms of uremia and died in coma within a few days. This is the only instance in all of our series of any atypical phenomenon, and in view of the fact that many of these advanced cases die within a month or so after radiation from the ultimate results of the disease, we see nothing noteworthy in this one event."

"The second application is made in the same way. Subsequently we try to see these cases or secure a report from the family physician or the patient every three months."

"From our summary of 209 cases, we find no cause for discouragement, for we have seen splendid palliative results from radiation, and we hope that with a further development of technique, cancer of the cervix may be removed from the surgical domain. In this possible transfer we are sure we shall find few dissenters among surgeons, for certainly we have no grounds for optimism from a radical operation in the pathetically small percentage of operable cases. For every case which may with reason be submitted to operation at least ten will fall by the wayside because they apply for help too late. To these wretched sufferers radium offers a palliative boon and even a possibility of cure. In cancer of the fundus the results in favor of hysterectomy are too satisfactory to be jeopardized by the use of radium, although in at least four cases we have witnessed a very favorable outcome in patients in whom there were grave contra-indications to surgical measures. In two instances a cure appears to have been effected. For patients, therefore, suffering with complications prohibiting an operation radiation offers a decided hope, for in no anatomic situation may we so certainly secure the full force

of the radium without ill results. The radiations are confined to the fundal cavity and the muscular uterine walls shield other organs from injury. Thus far, there has apparently been no attempt to find a uniform plan of application, each reporter has apparently been no attempt to find a uniform plan of procedure, each reporter of his experience having followed a method differing from his colleagues. It seems to us that this Society should take cognizance of this matter and appoint a committee to bring forward standardized suggestions."

* * * *

Henry Schmitz, A.M., M.D., F.A.C.S., (Chicago). The Biological Reaction of Carcinoma Cells Produced by Radium Rays. The Technique of Radium Therapy in Gynecology. The American Journal of Roentgenology, vii. 52-56, January, 1920. Read at the Third Annual Meeting of the American Radium Society, Atlantic City, N. J., June 5, 1919.

"A study of the biological reaction of tissues to radiation enables us to interpret correctly their therapeutic value and assists us in the choice of the quantity and quality of rays to be employed."

"Since the therapeutic action of radium is not only local but is also general or constitutional, a correct knowledge and interpretation of the local and systemic reactions are necessary and very important. Clinical observations of the latter furnish a guide to the determination of indications and contra-indications to radium therapy."

"Not only that—a knowledge of the biological as well as the therapeutic, i.e., local and systemic reactions, will materially aid us in the correct development of the technique for the application of the rays and in the probable prognosis of radiation treatment."

"We must always realize that success in cancer treatment can be attained only by the total eradication or degeneration of all cancer cells present in the body of a victim of the disease. This principle must be observed if we are to expect results, whether the means chosen are surgical or radiological. The danger in the treatment of cancer with surgery consists in the fact that we cannot always remove all tumor tissue. The vestiges left grow after such treatment with an increased rapidity, and by auto-transplantation cause secondary growths in different parts of the body. The danger in the treatment of cancer with radio-active substances arises from the fact that proliferation is enormously stimulated if we cannot rapidly destroy all the pathological cells. An accelerated proliferation increases the danger of the formation of metastases."

"H. Dominici has made extensive and valuable researches of the biologic action of radium rays. He applied 100 mg. of pure radium sulphate in a flat applicator of 5 sq. cm. to the skin of a healthy animal. Within three weeks after the application he observed three varieties of change. The epidermis and cutis which had absorbed all of the alpha and soft beta rays showed a necrosis and destruction of these structures. The subcutaneous tissue and fasciae which were subjected to the action of the medium beta rays were undergoing an intensive proliferation and retrogression to the embryonic state. The hard beta and gamma rays had become absorbed in the aponeurosis, muscle and even osseous tissues which evidenced metabolic changes. In from five to six weeks after the application of the radium the epidermis and cutis had regenerated, while the other tissues did not return to a normal state for from six to eight months."

"This observation demonstrated the variety of action of radium rays: necrosis, stimulation of cell proliferation, embryonal retrogression, and metabolic changes. It also showed the different behavior of various elementary cells toward the rays, which was termed by Dominici 'receptivity' or 'sensitiveness,' and by Colwell and Russ 'selective absorption.' Based on these facts Bergonie and Tribondeau formed the law that 'immature cells, and cells in an active state of division are more sensitive to rays than are cells which have already acquired their fixed adult morphological or physiological characters.' "

"The degree of selective absorption of rays by the living cell depends upon the particular phase of its life cycle, its species, as well as the age of the host whom it inhabits. Cell elements which are embryonal or undifferentiated are destroyed by a radiation which would cause only a slight reaction in the surrounding mature or highly differentiated cells The basal cells of the epidermis and hair follicles, lymphoid cells and sex cells (as ova and spermatozoa) are readily killed by an amount of rays which would leave intact the neighboring mature cells."

"Selective absorption also depends upon the species of the cell, whether epithelial, connective tissue cells are less receptive than normal epithelial cells. Epithelial cells of the basal layer of the skin are less receptive than normal epithelial cells. Epithelial cells of the basal layer of the skin are less sensitive than those of the papillae of the hair follicles, although they are different kinds of the same species. Lastly, the tissues of a child are much more easily altered by radiation than corresponding tissue elements in the adult."

"These observations made on normal cells apply with equal force to abnormal cells and tissues, neoplastic as well as inflammatory."

"Remarkable examples of radio-sensitive tumors are ectodermal and basal-celled epitheliomata derived from the basal-celled layers of the epidermis, lymphadenomata originating from the embryonal lymph cells, sarcomata derived from embryonal connected tissue cells in which the connective tissue fibrillæ, cartilagenous and osseous tissues have undergone re-absorption, fibromata in which the fibroblasts are present in large numbers and do not develop into highly differentiated adult cells, and connective tissue fibers."

"On the other hand squamous-celled epitheliomata, fibrosarcomata, chondrosarcomata, osteosarcomata, and fibromata in which atrophic fibroblasts and abundant fibrous tissue have been retained, are very refractory to radiation."

"The action of radium rays on neoplastic cells is of an impeding, destructive and evolutional character. The radiation arrests the growth of the tumors before it destroys them or renders them harmless by an evolutional process or metaplasia. Arrest of growth results from a cessation of the function of mytosis or genocepter. Destruction of tumor cells is either a direct or an indirect process. In the direct form the tumor cells undergo necrobiosis. The cytoplasm and nucleus disintegrate, and the cells are absorbed by phagocytosis. In the indirect destruction a metamorphosis of the tumor cells precedes absorption. This consists in a hypertrophy of the cells, enlargement of the nucleus, nucleolus and even centrosomes, so they appear like pseudo-parasites, and achromatism, vacuolation and granulation of protoplasm."

"The evolutional influence of radium on tumor cells is evidenced by a retrogression, or stimulation of the embryonic tumor cells as they develop to maturity. To understand this process we must have a clear con-

ception of the formation, growth and function of a cancer cell. Tumor formation deprives the cells of their normal functions. They become 'strangers' to themselves and to the mature normal cells from which they originate."

"The growth of tumor cells is not only the result of a proliferation of a single embryonal cell group, but also depends on a retrogression or metamorphosis of normal mature cells to an embryonal phase after they have become included in the cancer tumor. By a process of evolution the embryonic abnormal cell is stimulated to grow and develop into a mature, highly differentiated normal cell, thus becoming benign."

"Let us conclude with Colwell and Russ: Very rapidly growing cells are the most affected of any by radiations. However, different rays give rise to quite different effects upon one and the same variety of cell, they have a 'differential' action and a careful distinction should be made between the 'differential' action which different rays have upon the same variety of cell, and the 'selective' action which the same kind of radiation has upon the many different varieties of cells."

"Microscopic examination of tissues exposed to hard beta and gamma rays reveals the following facts: Soon after exposure, a serous infiltration, an enlargement of the cell nucleus and cell body, and a swelling of the endothelial cells lining the capillaries are seen. The lumen of the latter decreases in size. Within seven to eight days a degeneration of the cell nucleus is evidenced by a cessation of mitosis, a pyknosis, cytolysis and achromatism, while the protoplasma evidences vacuolation and granulation. A reactive inflammatory process also appears characterized by a lymphocyte and leukocyte infiltration and the appearance of numerous young fibroblasts. It seems as if the compact tumor masses break up in small particles separated from each other by this young connective tissue. The cell debris is rapidly cleared away by phagocytosis. The fibroblasts mature into connective tissue. It would appear as if the tumor had actually vanished. However this is not the case. On more careful examination, especially in regions more distant from the radium, epithelial cells are still seen, sometimes isolated, at other times in small nests that exhibit all stages of degeneration. Whether they are dormant or absolutely harmless or dead, of course, cannot be stated. However if radiation is not continued they may again assume renewed activity leading to a recurrence.

Prime considers that these degenerative processes affect the cell nucleus in preventing mitosis. Such radiumized tissue will not grow when inoculated in mice. Radium does not kill the cell outright, but injures the nucleus in such a manner as to prevent further division, which must eventually result in the death of the cell if its energy is expended in growth and division and not in a purely mechanical function.

Technique. In America the Wertheim operation has never been distinctly popular because of the feeling that the additional cases saved by this method do not justify the higher mortality from the operation. From the economic standpoint it must be considered that a competent Wertheim operation is beyond the reach of the great majority of the population and that all the phases of the cost of acquiring technical skill should be counted in estimating its utility. Because of these considerations a marked change has occurred during the last few years in the aspects of surgical treatment of uterine cancer, most surgeons preferring to reduce the scope of operability, and others abandoning all operations for uterine cancer in favor of radium and x-ray treatment. Earlier diagnosis has

doubtless contributed to improving surgical statistics and is equally important for radium therapy. In these directions lies the hope of real advance in the therapeutics of uterine cancer.

The demonstrable reduction in size of a tumor of a kind not to be attributed to the natural processes of evolution of that tumor or its associated lesions, is the one essential feature of effective therapeutic intervention. Circulatory changes in the tumor, the relief from pain, the restoration of a secondarily impaired function and local healing, cannot be cited as indications of the specific curative action of the agent employed. The growth may continue to advance in spite of their presence. We should exclude from consideration all these secondary factors. The observation of the size of the tumor itself is the sole criterion on which we can place reliance in judging of the effect of therapeutic measures.

Accordingly we have attempted to evolve the technique of radiotherapy. The latter may be profitably divided into two parts: the dosage and the technique of application.

Dosage is a complex quantity and includes the quantity of radioactive material, the volume in which it is contained, or the area over which it is spread, the nature of the rays selected, and the time during which they are applied.

The radium tubes should contain approximately 50, 35, 25 or 15 milligrams element. The filters used for internal work can be filled with any combination of these tubes up to 100 milligrams. The 15 milligram element of radium is contained in a platinum needle with an iridium point. It may be thrust into the tumor substance, for instance, through the perineum into a lobe of the prostatic gland under guidance of a finger in the rectum, or into the substance of the tongue, the cervix, the paracervical tissues, etc.

"As the therapeutic action of radium extends for a radius of about 4 cm., from 50 to 100 mg. of radium element are inserted into the uterus, if that organ is the seat of a carcinoma. Should the uterine canal measure 3 inches in length, 75 mg. are deemed sufficient; if it measures 4 inches, 100 mg., and so on. The "bomb" may carry up to 100 mg. and is placed directly against the cervix and vaginal vault if an extensive involvement of the vaginal portion of the cervix and vault are present. The rays will cause a degeneration of carcinoma tissue within a radius of 1 cm. within eight hours, within 2 cm. within thirty-two hours and within 3 cm. within seventy-two hours, and so forth. Therefore a cervical or uterine growth is exposed to the action of the rays for seventy-two hours, 3 cm. being the average extent of an area which could be effectually influenced by radium rays. Extensive infiltrations of the parametria are punctured with a special trochar which enables us to bring the element directly into these masses. The tubes are left for a variable length of time corresponding to the extent of the area."

"The arrangement of the capsules is as follows: The radium is contained in silver or brass capsules of a wall thickness of 0.5 mm. These capsules are inserted into a filter made of brass of a wall thickness of 0.7 mm. The filter is then surrounded by a rubber tube (fountain pen filler) of 3 mm. thickness. A thread is attached to the filter cap, which is secured with a safety-pin to an abdominal binder."

"In noting results we observe: (1) the arrangement of the radium capsules; (2) the distance of the capsule from the tumor tissues; (3) the method of filtering; (4) the duration of each seance; (5) the interval between seances; (6) the histological structure of the tumor, if

biopsy is advisable; (7) the comparison by examination of the actual size of the tumor preceding each seance of treatment; (8) the visible effects of radium on the tissues, as erythema, burns and so forth; and (9) daily examinations of the blood, including a differential white count. These are of importance to interpret correctly the latent action of radium on tissues and constitution and to determine the curative or palliative efficiency of the agent."

"We observed in our earlier work that though we obtained a local regression of the tumor evidenced by local healing, reduction in size of the growth, normal findings on palpation as to position, movability, size, form, consistency and sensitiveness of all the generative organs, the growth would continue to grow or reappear with undesirable frequency at its periphery. Evidently the rays did not destroy the distant parts of the tumor. To overcome this difficulty we resorted to a simultaneous use of the roentgen rays, and have found in them an effective means of combatting the peripheral spread of the tumor."

"The technique of the roentgen rays therapy has been rendered so exact in its minutest details that carelessness or neglect are impossible. Three illustrations indicate the areas into which the chest, abdomen and sacral area are divided to provide multiple portals. To each square 50 milliampere minutes are applied. The Coolidge tube must take a spark of nine inches, the milliamperage being 4 to 5; the rays are filtered through 0.5 mm. of zinc or 3 mm. of aluminum; the secondary rays forming in the metal filter are arrested by the distance between it and the body surface, it being placed about half way between tube and body surfaces. The distance of the anode from the body surface is 21 cm. With such an arrangement we obtain about 6 E doses, i.e., 30 X or 15 H, within 10 minutes, if the pastille is placed above the filter and 1E if it is placed on the skin surface. According to Bumm's researches, 3 to 5 E doses will destroy carcinoma tissue within one centimeter from the body surface, but it takes 7 to 10 times this amount to obtain similar results near the posterior bony pelvic wall, the seat of the glandular metastases in cancer of the pelvic organs. By using multiple portals of entrance, 7 to 12 fields suprapublically—3 to 6 over perineum and sacrum and 2 over each greater sciatic foramen—we may succeed in obtaining the same therapeutic results in the tissues adjacent to the posterior bony pelvic wall as with radium locally. We must tilt the tube so it will always be directed to the same area within the pelvis. The number of fields must be determined for each individual case, and depends on the diseased organ, the extent of the infiltration of surrounding structures, the region of the body and the location of the regional lymph nodes. An interval of three weeks is observed between each course. The latter is crowded into the smallest possible space of time, that is, the treatments ar usually applied in one sitting. From three to four courses are given in each case."

"In conclusion I wish to recapitulate:"

"1. The biological reaction of cancer cells to radiation offers the best evidence of the therapeutic efficiency and curative possibilities of the gamma rays and the hard roentgen rays."

"2. The efficacy of the treatment must be based on the demonstrable reduction in the size of a tumor and not on the local changes and improvement in the subjective condition of the patient."

"3. The evolution of a successful treatment must be guided by these observations, a correct dosage and a detailed and careful technique."

* * * *

C. W. Hanford, M.D., (Chicago). Large and Small Doses of Radium. Surgery, Gynecology and Obstetrics, 210-211, February, 1920.

"The writer has often stated, and other observers in the field of radium therapeutics have voiced the same thought, that radium is of distinct value in cases of inoperable cancer, particularly of the cervix uteri. And yet recent experiences have shown that some surgeons (?) either do not know when a case is inoperable or use the knife, regardless of consequences. I consider that this attitude is as open to criticism as that of employing escharotics and other agents, after it has been plainly demonstrated that a patient has cancer."

"If the surgeon is so anxious to use the knife in a case of cancer of the cervix uteri when possibly the vaginal wall is involved, he should have enough regard for the patient to employ radium in the cervix and vagina until the local lesion is cleared up, at which time the chances for good end-results have increased many times. The time has passed when there is any guess work as to the action of radium rays in malignancy."

"Given a case of carcinoma of the cervix, if the patient is not too much weakened by the disease, we can almost promise a clearing up of the local lesion, with the unpleasant accompanying conditions—bleeding, odor and pain—after administering a dosage of 4,000 to 5,000 milligram or millicurie hours."

"I am sure that all who have followed radium therapy closely are of the opinion that when the diagnosis of cancer has once been established, it is absurd to temporize with small doses and short applications of radium. It is vitally imperative to strike hard when using radium in malignancy."

"If we have a case of cancer of the tonsils, we should not think of giving less than 1,200 to 1,500 milligram hours; and this should be given in a period of two days at least, better at one session. This means if we are using a 50 milligram tube, it is to remain *in* situ at least 24 hours. And again, the tube or needle should not be merely placed against the growth; it should be sunk into the center of the growth and fastened there."

"Whenever the dosage and time referred to above is used, there is naturally a slough of tissue in the immediate vicinity of the radium. This commences in about a week or ten days after the treatment, but as the walls of arteries and veins are very resistant to the rays of radium, danger from haemorrhage, due to the penetration of the walls of vessels, need not concern us."

"An illustration of the value of striking hard with radium after the diagnosis of cancer is confirmed by microscopical section, the following case will serve."

"The patient, age 47, a farmer from Janesville, Wisconsin, was referred to the writer by T. B. Wiggin, of Chicago. He gave a history of tonsillar affection that commenced 6 months ago. The soft palate became invaded, until finally the existing hole would easily receive an English walnut. This cavity extended back and up some distance. Besides this, one of the cervical glands on the right side of the neck just under the ear was as large as a hen's egg. The patient was totally deaf in the right ear. He had lost 40 pounds in weight and was very weak."

"One hundred and eighty milligrams of radium screened to exclude the beta rays were placed in the cavity in the soft palate and stitched in. The radium was left in place for 9 hours. No treatment was given

the next day, but the day following, the patient received the same dose for 5 hours. Again a day was allowed to elapse and the day after, the treatment lasted 6 hours, making a total of 20 hours, or 3,600 milligram hours, over a period of 5 days."

"The patient went home, returning to the hospital after 12 days. The cavity in the soft palate had markedly narrowed, there was no odor, and even after examination, there was no bleeding. The gland on the side of the neck had diminished one-half. At the first examination, an enlarged gland in the submaxillary region was found; this had entirely disappeared. The patient felt much stronger and more hopeful. He was now given one application in the cavity of 110 milligrams for a period of 6 hours. Also James N. Neff ligated the external carotid, even though improvement had been so marked after the first treatments."

"The patient returned home and did not come back to the hospital for a month. He had gained 25 pounds in weight. The hole in the soft palate had nearly closed. There was no sign of the large gland. The patient said he had been doing all of his farm work and never felt better in his life."

"Prior to receiving radium treatment he had sought aid at the largest medical and surgical institution in the North West, but was given no satisfaction. A recent letter states that he is nearly back to his normal weight."

"Now if temporizing methods had been employed in this case by using 25 or 50 milligrams of radium, the final good result would have been very slow in coming, and I am very doubtful if a definite result would have ever been gained."

"Massive doses. The writer believes that if he were in possession of 2 or 3 grams of radium, as is the case at a few eastern institutions, he would always speak of massive doses for short periods, for there is no doubt that there is considerable satisfaction in having at hand this large amount of an ultra expensive element. But from a therapeutic standpoint, the application of anything over 200 milligrams of radium element to any one point, is simply for the purpose of shortening the hours of exposure. If we wished to give a uterine fibroid a 1,500 milligram hour irradiation, we would use 100 milligrams of radium for 15 hours. Or if we possessed 500 milligrams in one tube or 500 millicuries (emanation) in a needle, it would be in position but 3 hours."

"The writer will concede this point: that in deep malignancy the employment of any dose less than 50 milligrams for a series of hours, is often harmful, in that there is not enough power in the gamma ray content to act as a lethal agent against cancer cells. But, on the other hand, in a zone slightly removed from a small dose of radium, the cancer cells will be whipped into activity, and we have as a result a more grave condition to deal with than if nothing had been used."

"The fact that the use of radium in suitable cases does not entail a great loss of tissue commends its use in cases where the radical use of the knife would cause great disfigurement."

"The writer's position as regards cancer of the breast is, he believes, held by all who have had more than a passing acquaintance with radium. The surgeon should always have first chance in these cases, but I still believe that the prophylactic treatment with radium at the time of the operation or within a few days after should not be overlooked."

"It is natural that only by experience and close observation, can the best results be obtained from so powerful an agent as radium. Because of its innocent appearance, and until recently, lack of information as to dosage, etc., many have been led to believe that they can place the tube anywhere, for indeterminate hours with no fear of untoward results. They are surprised, when the reaction sets in in a week or ten days after treatment, to note an ever increasing area of redness and final destruction of tissue, when the proper application should have produced no more perhaps than a redness. Therefore, I am sure that all radium therapeutists will agree with the writer that each case should be viewed by one thoroughly acquainted with the action of the rays of radium. We have all seen the havoc wrought in the vagina by the too long application of radium and improper screening, thereby causing rectovaginal and vesicovaginal fistulae."

"In treating new-growths with radium, there are some things we cannot expect to accomplish. These include—

"Very little benefit in cancer of the tongue, if the glands of the neck and submaxillary region show involvement."

"Only temporary improvement in carcinoma of the rectum, especially if of the hard non-vascular type. In some instances the vascular type, if in the middle and upper third, respond fairly well."

"Recurrent cancer of the breast if submitted to radium element some months after the operation, shows little if any improvement, because the invasion of the lymphatic system is extensive. The time to use radium in breast cancer is immediately after the operation."

* * * *

Echlin S. Molyneux, M.R.C.S., (Leamington, Eng.). Radium in the Treatment of Tuberculous Adenitis. The British Medical Journal, 705-706, November 29, 1919.

"The therapeutic properties of radium have always been a fascinating subject, both to the medical profession and the laity, and the medical profession have by no means, I think, reached the limits of the subject yet."

"During 1913-14 I thought I would see what could be done for tuberculous glands by radium. As a result I am convinced that the day of radical operation will soon be past, that it will no longer be necessary to send children thus affected for prolonged periods to the seaside, and that the unsightly scars which disfigure the necks of so many girls can now be avoided. Radium is, if properly used, a safe, and as far as I can see a certain, cure, whether for an early or an advanced case of tuberculous glands. Within the period named I treated between twenty and thirty cases of every grade with radium. In every case the swellings and even old sinuses faded away. Unless there were already sinuses present, no scars were left. The skin was in some a little red for a few weeks from the action of the radium, but this always disappeared."

"In no case was any ulceration caused. It is unnecessary to describe all the initial experiments and the doses used. As a result I find as follows:"

"Fifteen milligrams of radium bromide, spread out on a flat circular applicator 1¼ in. in diameter,* and mixed with a special varnish to

*Approximately quarter strength in terms of units used in this country.—Ed.

keep it even and prevent loss, is sufficient for this kind of treatment. The applicator has a screen of silver 1 mm. thick, and a piece of thin gutta-percha tissue tied over the whole to prevent soiling of the radium. The applicator is strapped on over the tuberculous glands. I have found ten hours a suitable time for each application of the above strength—that is, 150 milligram† hours. The applicator is applied when the patient goes to bed and taken off in the morning. A different gland or group of glands can be attacked at each sitting till all have been covered, and the course then started again."

"The patients usually have had two applications a week. Nothing was noticed for from a week to ten days, but from that time a gradual shrinkage of the glands was observed till nothing could be felt except a few fibrous nodules. I continue the treatment till all signs of trouble have disappeared. In very bad cases I usually gave in addition a few applications three months later, but doubt whether this is really necessary if the first treatment is properly carried out."

"Since my demobilization from the R.A.M.C. I have had an opportunity of inspecting many of the patients I treated in 1913-14. In none of them can I find a trace of any further trouble, nor have I heard of any I have not actually seen having any signs of recurrence. Evidently, therefore, the cure is unusually a lasting one. Should a case recur, I have no doubt that a further course of treatment would restore the patient to health again."

"I will briefly quote three typical cases to illustrate the different degrees of the disease treated."

"Case 1. A boy aged 4. Early tuberculous glands of the left tonsillar and carotid region; no obvious signs of softening."

"He had five applications of 15 mg. of radium, ten hours each application, at intervals of seven days. At the end of this time all signs of the disease had disappeared."

"Case II. A woman, aged about 30, had had a swelling on the right side of the neck for a year. It had been treated by iodex tonics, change of air, and all the usual remedies. When I first saw her the mass of glands was nearly the size of an orange, and there were marked signs of caseation; I was, in fact, afraid lest they would break down and suppurate through the skin before the action of the radium could have much effect. Her general health had suffered considerably."

"I treated her twice a week with 15 mg. of radium, ten hours each time for ten sittings. There was an interval of a month, while she was paying a visit, in the middle of the treatment. At the end of that time the neck was perfectly normal. Fortunately the radium began its work before surface suppuration had occurred. I saw her three months later, and she was thoroughly restored to health and there were no signs of there ever having been any trouble in the neck. To take no risks I gave her three more similar applications."

"Case III. A boy, aged 4, one of a large family, nearly all of whom had suffered from tuberculosis; several had died. His mother and one or two uncles and aunts had died of phthisis. When I first saw him he had extensive tuberculous adenitis on both sides of the neck. The glands had suppurated, and sinuses secondarily infected were present."

"I gave him ten applications of from eight to twelve hours each,

†Author uses bromide as unit, whereas radium element is standard in U. S.—Ed.

twice a week. On several of these occasions, after four hours the applicator was moved to cover another group of glands, and so on. The same strength, 15 mg. of radium was employed. At the end of this treatment all the sinuses had healed, and the masses of glands had shrunk till only a few fibrous nodules could be felt. The boy had also improved much in health, and when I saw him a few months later one would hardly recognize him."

"Carious teeth or unhealthy tonsils and adenoids, if present, must be dealt with at the beginning of the treatment, as it would be folly to cure the existing glands and leave a future source of infection behind."

* * * *

Ernest Charles Samuel, M.D., (New Orleans). Three Years' Experience with Radium in Cancer of the Uterus. The American Journal of Roentgenology, vii, 42-51, January, 1920. Read at the Third Annual Meeting of the American Radium Society, Atlantic City, N. J., June 5, 1919.

"In the last two years, I have limited my exposures for malignancy of the uterus to twelve hours, not using over 50 milligrams of the element, the dosage being 600 mg. hours for each treatment. My first year was very disastrous—I think I was over-enthusiastic, using 150 mg. of the element for 12 hours and in a few cases for a longer time. Seeing the marked benefit from the smaller dosage, I thought larger doses and heavier screening would accomplish better results. It took me about one year to get my bearings. After seeing quite a number of fatalities which I knew were due to overdosage, I wish to make the plea before this meeting for smaller doses and at least a ten-day interval between exposures, filtering more at each exposure and stopping for four weeks at the end of the third exposure. I have been able to accomplish just as good results with this method as I did with the larger dosage, and with more comfort to the patient. The patients are not toxic after the smaller dosage; the bladder symptoms, I was having, are eliminated; no proctitis is seen—all of which we know make the patient more miserable than the growth. I generally give three cycles of three treatments each with, as stated before, four weeks' rest after each cycle. At the end of three months the treatments are resumed. A piece of tissue is always removed or a diagnostic curettage is done before the treatments are begun; no cases are received unless they will submit to the procedure. At the end of three months, a piece of tissue is again removed, if possible, and studied by the pathologist. While I realize this does not mean much in the prognosis, because in the large majority of cases that we see, the parametrium is undoubtedly involved, it acts as a control to further treatments."

"There is no doubt that the wide publicity that has been given the subject has done some good in leading patients to consult the doctor earlier; but I am sorry to say the profession is largely to blame for the hopeless, inoperable cases that we see daily. Of the patients who apply to us for treatment, at least 80 per cent. are already in the inoperable stage; quite a few will give a history of having consulted their family physician and having been given a douche; in other cases ergot was prescribed and they were told it was the "change of life," and not even a vaginal examination was made. When the doctor finally discovers the true condition and the patient is rushed to the surgeon or the radiotherapeutist, and when surgery or radium fails, both are condemned."

"The entire problem that must be considered in successful treat-

ment of carcinoma of the cervix must be based upon the invasion of the new growth. The radical operation has proved that the hopeless cases are those of the metastatic type, and everything must be directed toward the local vaginal and cervical disease; if the growth has invaded the paramentrium and around the uterus also—if the iliac glands are involved—the case must be considered hopeless and radium gives the greatest percentage of relief to the patient, controlling the local disease, stopping the discharge, pain and hemorrhage."

"The inoperable cases are operated on without delay, and though radiation is given just as soon after as possible, with radium and deep roentgen therapy, we do not give a preliminary treatment before operation, as the operators have found considerable difficulty with the tissues that have been radiumized. It is very difficult to control hemorrhage, as the parts are very friable; even the cases that are inoperable when first seen and by treatment are apparently rendered operable, are let alone. Recently Kohlmann, in the Gynecological Service at Touro Infirmary, has been making an abdominal section and tying the iliacs, and, as soon as the patient is over the surgical shock, radium has been introduced into the vagina and been placed against the growth in the usual way; the cases seem to do better by this plan. He is working along the old theory of cutting down the blood supply to the parts and assisting radium in that way."

"Radium, in our hands, has offered the most helpful outlook for the palliation and, occasionally, for the cure of cancer of the uterus; but I think the majority of the profession expect too much in the form of absolute cures. Such has not been our experience; in fact our results are disappointing, as only a small number of our cases have remained well for over two years. All the patients apparently do very well for the first eight to twelve months, and during this time it is very hard to find any evidence of the growth by inspection—vaginal or abdominal palpation. They will start to complain of vague abdominal pain; upon examination we find marked evidence of a recurrence, and in our experience it is useless to resume the use of radium, as in the majority of cases it is like adding coal to the fire.

"I regret to have to report the results of our observation in this particular field as I must admit I expected more. Reports from other clinics are more encouraging, I think, than ours—why, I do not know!"

"The youngest patient treated for malignancy of the uterus was twenty-four years old. We were able to control the growth for a while but, as I said before, I was too enthusiastic and gave her 3,200 mg. hours in three treatments; she developed a septic diarrhea and died in ten days. No postmortem was allowed. Our oldest patient was seventy-nine years old; I gave her only one treatment of 425 mg. hours and she improved wonderfully and is alive today—that was one year ago. The next oldest was seventy-eight years old with a growth in the cervix; I gave her 2450 mg. hours in four treatments and she is well today. The patients beyond 60 years old seem to do better. Our average age has been between 45 and 55, and the average duration of life, after radium treatment was begun, has been 18 months to two years. The cases treated with the Percy cautery do not do well with radium treatment, as they are already toxic and any addition causes trouble. The average number of treatments given was six in two cycles of three each, using 50 mg. for twelve hours, which gives 3600 mg. hours."

In tabular form brief histories are given for 124 cases.

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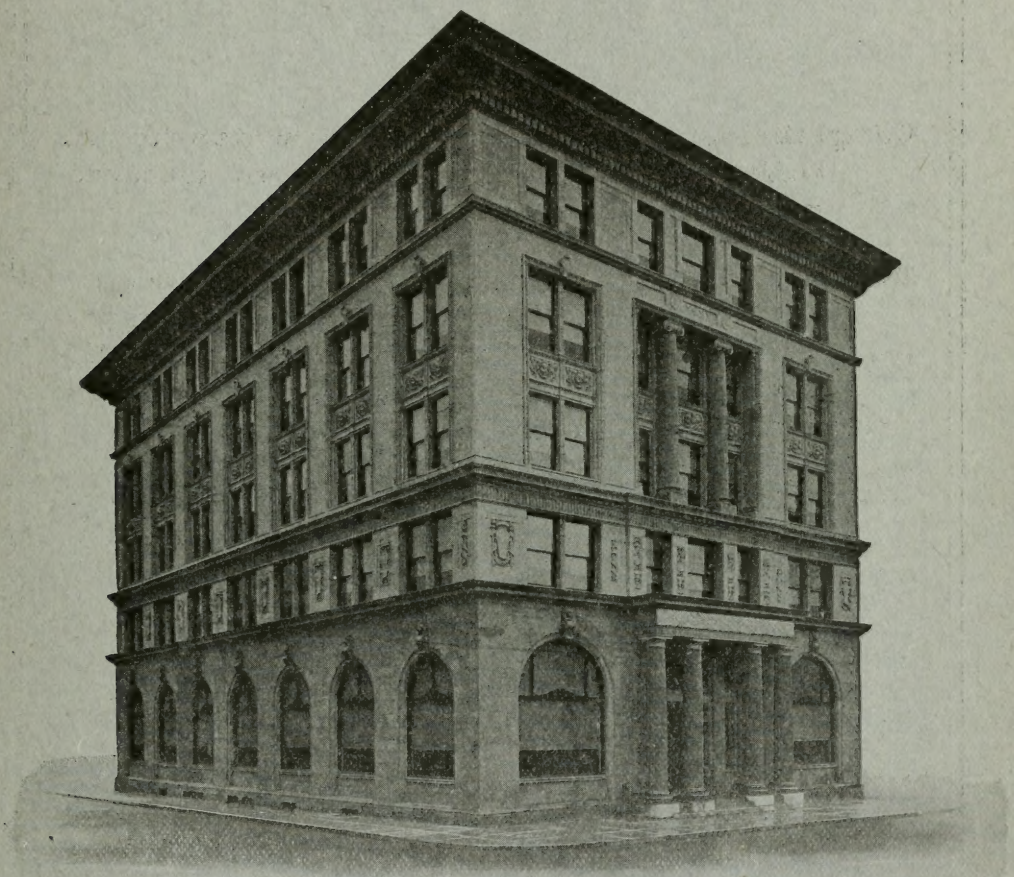

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